Research Highlights

Sharon Lobert, RN, PhD
Associate Editor

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Epidemiologic Research

Aspirin May Increase the Risk of Pancreatic Cancer

The longest-running major women's health study is the Nurses' Health Study that was initiated in 1976 and involved 88,378 women who initially were cancer free. Researchers from Harvard University Medical School in Boston, MA, presented the results of an analysis of these data examining the relationship between aspirin use and pancreatic cancer risk. During the 18 years of follow-up, 161 cases of pancreatic cancer were documented. Aspirin use was assessed biennially from 1980. For women who reported taking two or more aspirin tablets per week for 20 or more years, the risk of pancreatic cancer relative to those who did not take aspirin was increased by 58%. Consistent aspirin users, defined as those who reported aspirin use on at least two of three consecutive biennial questionnaires and were taking 14 or more aspirin tablets per week, had nearly an 86% increased risk of developing pancreatic cancer. Those taking 6–13 tablets per week had a 41% increased risk for pancreatic cancer. The researchers suggested that women need to consult with their healthcare providers regarding aspirin use. Extended aspirin use may increase the risk of pancreatic cancer significantly in women.

Clinical Research

Weight Loss May Lower the Risk of Breast Cancer

Researchers from South Manchester University Hospitals in the United Kingdom presented the results of a trial of diet regimens for women with a family history of breast cancer. A total of 79 women who had gained significant amounts of weight as adults were enrolled in the study. The women were assigned to either a calorie-restricted and exercise weight-loss program or a standard diet with only exercise advice. Biomarkers for breast cancer risk were measured across both groups. The researchers measured body weight, waist circumference, percentage of body fat, total subcutaneous and intra-abdominal fat, insulin, testosterone, and sex hormone binding globulin (which affects estrogen levels). The data were analyzed to evaluate the effects of losing more than 5% or 0%–5% of body weight. According to the scientists, the data indicated that a positive benefit existed in terms of levels of biomarkers for breast cancer risk for the women in the study who lost 5% or more of their body weight.

Lower Levels of Dense Breast Tissue Are Associated With Higher Physical Activity

Dense breast tissue is associated with an increased risk of breast cancer. Data from the Health, Eating, Activity, and Lifestyle Study indicate that lower amounts of dense breast tissue are associated with higher physical activity levels, suggesting a link between physical activity and breast cancer risk. Researchers from Yale University in New Haven, CT, examined data collected from 1,223 women on physical activity, diet, weight, hormones, breast density, and other factors that affect breast cancer prognosis among newly diagnosed patients with breast cancer. Physical activity and breast density data were obtained from information and mammograms from the year prior to diagnosis. The analysis demonstrated a statistically significant 17% difference in breast tissue density comparing the least active and most active premenopausal women with body mass index (BMI) scores less than 30. Postmenopausal women or those with BMI scores greater than 30 did not show this association. The authors concluded that this study provides evidence of the benefit of regular exercise and could be used to motivate women to be more physically active.

Lower Breast Cancer Risk Is Associated With Intake of Fruits and Vegetables

Researchers from the School of Medicine at Oregon Health and Science University in Portland presented results from a study that suggest that women who consume fruits and vegetables daily may have significantly lower breast cancer risk. In this study, the dietary habits of 378 women in Shanghai, China, who had been diagnosed with breast cancer were compared with those of 1,070 age-matched women who did not have breast cancer. An in-depth food frequency questionnaire that recorded factors such as food groups and caloric intake was used to assess dietary intake. The consumption of four or more servings of fruits and vegetables per day was associated with reduced breast cancer risk. No association existed between the intake of soy or soy products and breast cancer risk. The researchers concluded that this study reinforces the importance of fruits and vegetables for disease prevention.

Green Tea Polyphenols May Protect Against Liver Cancer in High-Risk Patients

DNA damage by oxygen free radicals is associated with tumor formation. Urinary 8-OHdG can be used as a measure of this damage. Green tea polyphenols (GTP) inhibit a variety of tumors in model systems, including liver tumors. Researchers from Texas Tech University in Lubbock investigated the effect of GTP on liver cancer biomarkers and urinary 8-OHdG. In their study, 124 people aged 20–55 with positive reactions for hepatitis-B surface antigen and aflatoxin, a poisonous substance produced by mold, were assigned randomly to three groups. Group 1 received low-dose GTP (500 mg, n = 42), group 2 received high-dose GTP (1,000 mg, n = 41), and group 3 served as the control, receiving a placebo (n = 41). Urine samples were collected at baseline, one month, and three months to assess urinary 8-OHdG and GTP biomarkers. Blood and urine samples were collected at baseline, one month, and three months to assess aflatoxin biomarkers. Baseline GTP biomarkers were similar in all three groups. At one and three months, urinary GTP biomarkers were elevated significantly in both treatment groups compared to the control group. In addition, urinary 8-OHdG and the aflatoxin biomarkers were greatly reduced in the GTP-treated groups at three months compared to the control group. The results suggest that GTP may play a role in liver cancer prevention.

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Basic Research

Ginger May Inhibit Growth of Colorectal Tumors

Researchers from the Hormel Institute at the University of Minnesota in Austin presented the results of a study of the effects of ginger compounds on colorectal tumors in mice. In this study, mice were fed 0.5 mg of [6]-gingerol (n = 20) or 0.001% ethanol in water (control, n = 20) three times a week for two weeks before and then the same amounts after implanting human colorectal tumor cells. Mice were weighed and their tumors were measured twice each week. The mice were athymic nude mice, incapable of rejecting human tumor cells. Tumors were found in both groups at day 15 after tumor implantation. A significant difference existed in the number of tumors in the control and treatment groups, 13 and 4, respectively. In addition, the tumor sizes differed between the two groups. By day 49, all the control mice had tumors that measured at least 1 cc^3; however, in the treatment group, only 11 mice had tumors of that size. The mice that received [6]-gingerol survived significantly longer than those in the control group. The researchers concluded that ginger compounds may be effective chemopreventive or chemotherapeutic agents.

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Clinical Research

Tyrosine Kinase Inhibitor SU11248 Has Biologic Effects in Advanced Malignancies

Researchers from the Centre for Developmental Cancer Therapeutics in Melbourne, Australia, and Pfizer Inc. in Nerviano, Italy, and St. Louis, MO, presented the results of an open multicenter trial of SU11248 for patients with a variety of tumor types, including colorectal, melanoma, sarcoma, and renal. SU11248 is a tyrosine kinase inhibitor that targets the platelet-derived growth factor and vascular endothelial growth factor (VEGF) receptors KIT and FLT3. These molecular targets are known to be important for intracellular signaling that helps cells and blood vessels grow. Positron emission tomography (PET) scan changes, conventional responses, and biomarkers were analyzed to evaluate the agent's efficacy. A total of 41 patients (24 males and 17 females) with a median age of 57 (range = 18–79), median Karnofsky Performance Score of 90 (range = 70–100), and a median of two prior treatments (range = 0–8) received a starting SU11248 oral dose of 50 mg per day in six-week cycles (four weeks on and two weeks rest). The most common toxicities were lethargy, thrombocytopenia, neutropenia, odynophagia, pigmentation of the skin, and depigmentation of the hair. Twenty-seven patients (66%) completed the 12-week study. From PET scan evaluation, 34% of the patients had a clinical benefit from SU11248. Rapid shrinkage of some tumors occurred. More frequently, a central necrosis of the tumor with a rim of persistent malignancy was observed. Rapid regrowth of some tumors was observed during the break periods in some patients. Plasma VEGF levels were increased, suggesting that SU11248 was modulating the tyrosine kinase targets. The researchers concluded that SU11248 has biologic effects on tumors and that further studies of the correlations among efficacy, toxicity, and drug exposure are needed.

Phase I Trial Demonstrates Activity of Novel Enzyme Inhibitor

Suberoylanilide hydroxamic acid (SAHA) inhibits the activity of an enzyme that allows "unwrapping" of DNA, permitting expression of genes important in cell proliferation. Preclinical studies suggested that SAHA can slow tumor growth. Researchers from Memorial Sloan-Kettering Cancer Center in New York City and Aton Pharma, Inc., in Tarrytown, NY, presented the results of a phase I trial examining the safety and activity of SAHA for patients with advanced solid tumor and hematologic malignancies. A total of 60 patients were entered in the trial that evaluated three oral dosing schedules: once daily, twice daily, or twice daily for three consecutive days every week. The recommended doses for phase II trial are 400 mg every day, 200 mg twice a day, or 300 mg twice a day for three consecutive days each week. The dose-limiting nonhematologic toxicities were anorexia, dehydration, diarrhea, and fatigue. The most common hematologic adverse events were grade III anemia and grade III thrombocytopenia. The toxicities were reversible upon stopping the drug. Reduction of disease was observed in seven patients. Test of peripheral blood showed that SAHA was active at its target.

Novel Ras Kinase Inhibitor May Slow Renal Tumor Growth

A novel agent, BAY 43-9006, inhibits the enzyme Ras kinase that is important in regulating tumor cell proliferation. Ras kinase also may inhibit the growth of new blood vessels needed for tumor development. Phase I data showed that BAY 43-9006 induced partial response in patients with hepatocellular and renal cell carcinoma (RCC) with a manageable toxic profile: hand-foot syndrome, rash, fatigue, and diarrhea. Researchers from the University of Chicago in Illinois presented the results of a multicenter phase II trial with patients with advanced refractory progressive solid tumors. During a 12-week induction phase, all patients received 400 mg BAY twice daily. At the end of the induction phase, patients who demonstrated a response to the drug with less than 25% tumor shrinkage were randomized into one of two groups to receive 400 mg BAY every 12 hours or a placebo. Those who demonstrated greater than 25% tumor shrinkage continued on BAY in an open label phase until disease progression or toxicity developed. Over nine months, 290 patients enrolled in the study. The toxicities were similar to those previously reported. Tumor regression was observed in several types of cancers: colorectal, melanoma, thyroid, sarcoma, pancreatic, and RCC. Of the 18 patients with RCC who were evaluable, 8 demonstrated tumor shrinkage greater than 25% and 7 were randomized into the BAY versus placebo arms of the study. The study is continuing, and analysis of the data from the randomized patients has not yet been done.